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(54) Title: COMPOSITIONS FOR THE TREATMENT OF AUTOIMMUNE DISORDERS

(57) Abstract: A method of inducing tolerance to an antigen in a patient, the method comprising administering to the patient an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof. Preferably, the agent which raises the effective cAMP concentration in a monocyte cell is a prostaglandin or agonist thereof which stimulates cAMP production in a monocyte. Optionally, the antigen to which it is desired to induce tolerance, or a derivative thereof, may also be administered.

WO 2004/035083 A3

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/04537

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/19 A61K31/5575 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61P A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, FSTA, CHEM ABS Data, PAJ, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STEINBRINK KERSTIN ET AL: "Induction of dendritic cell maturation and modulation of dendritic cell-induced immune responses by prostaglandins" ARCHIVES OF DERMATOLOGICAL RESEARCH, vol. 292, no. 9, September 2000 (2000-09), pages 437-445, XP0001180090 & ISSN: 0340-3696 the whole document ----- -/-	1-81



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

15 September 2004

Date of mailing of the international search report

05. 10. 2004

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/04537

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PIQUET-PELLORCE C ET AL: "PROSTAGLANDIN-E-2 POTENTIATES GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR-INDUCED HISTAMINE SYNTHESIS IN BONE MARROW CELLS ROLE OF CYCLIC AMP"</p> <p>LIFE SCIENCES, vol. 48, no. 25, 1991, pages 2377-2382, XP0001180093 &amp; ISSN: 0024-3205 abstract</p>	1-81
X	<p>KALINSKI P ET AL: "Dendritic cells, obtained from peripheral blood precursors in the presence of PGE2, promote Th2 responses."</p> <p>ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY. 1997, vol. 417, 1997, pages 363-367, XP0009027784 ISSN: 0065-2598 cited in the application abstract</p>	1-81
X	<p>ICHIMURA HIROSHI ET AL: "Differentiation of a cell line of human cervical argyrophil small cell carcinoma to macrophage lineage cells"</p> <p>JAPANESE JOURNAL OF CANCER RESEARCH, vol. 90, no. 5, May 1999 (1999-05), pages 523-529, XP002294672 ISSN: 0910-5050 abstract</p>	1-81
X	<p>US 6 010 905 A (SCHWARTZ GRETCHEN N ET AL) 4 January 2000 (2000-01-04) examples 20,23 claims 16,18 abstract</p>	1-81
X	<p>US 6 458 585 B1 (ALZONA MORTIMER T ET AL) 1 October 2002 (2002-10-01) abstract claims</p>	1-81
X	<p>US 5 891 432 A (HOO WILLIAM S00) 6 April 1999 (1999-04-06) abstract claims</p>	1-81
X	<p>WO 99/12563 A (US HEALTH ; BELYAKOV IGOR M (US); BERZOFKY JAY A (US); DERBY MICHAEL) 18 March 1999 (1999-03-18) abstract claims</p>	1-81
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/04537

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/64260 A (INST NAT SANTE RECH MED ; UNIV PASTEUR (FR); CENTRE NAT RECH SCIENT : (F) 2 November 2000 (2000-11-02) claims -----	1-81

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/04537**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-35 and 73-81 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-81 (all in part)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 1-35 and 73-81 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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## Continuation of Box I.2

Claims Nos.: 1-81 (all in part)

The functional definition "an agent which raises the effective cAMP-concentration in a monocyte" is not a clear, structural definition of a substance (Art. 6 PCT). The search was therefore limited to the agents as defined in claim 2-6.

The search of the unclear therapeutical definitions "inducing tolerance to an antigen in a patient", "stimulating or enhancing granulysin expression in the macrophage/monocyte lineage" and "stimulating or enhancing IL-10 expression in, and secretion from, cells of the macrophage/monocyte lineage" (Art. 6 PCT) were restricted to those diseases mentioned in claims 23, 27, 28, 30 and the virus diseases in claims 75-77.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/04537

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